PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/006492	16.06.2004	30.07.2003

International Patent Classification (IPC) or both national classification and IPC
G01N21/77, G03H1/02, A61B5/00, B29C35/08

Applicant
NOVARTIS AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Krametz, E

Telephone No. +31 70 340-2733

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing:

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 64

because:

☒ the said international application, or the said claims Nos. 64 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-49, 51-63, 65, 66
	No:	Claims	50
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-63 65 66
Industrial applicability (IA)	Yes:	Claims	1-63, 65, 66
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III.

According to Rule 67,1(iv) no international preliminary examination is carried out to the extent to which its subject matter is a method for treatment of the human body by surgery. An implantable ophthalmic, in particular subconjunctival device automatically implies surgery. Therefore claim 64 refering to use of an implantable device is not examined.

Re Item V.

1 The following documents are referred to in this communication:

D1 : US 2003/027240 A1 (LEDNEV IGOR K ET AL) 6 February 2003 (2003-02-06)

D2 : WO 99/33642 A (NOVARTIS ERFIND VERWALT GMBH ; NOVARTIS AG (CH); ZHANG XIAOXIAO (US);) 8 July 1999 (1999-07-08)

D3: US 6 303 687 B1 (MUELLER BEAT) 16 October 2001 (2001-10-16)

D4: US 3 993 485 (TOMLINSON III WALTER JOHN ET AL) 23 November 1976 (1976-11-23)

D5: US 2003/0107786 (BABLUMYAN ARKADY) 12 June 2003 (2003-06-12)

D6: US 5 835 245 (CHESAK ERIC ET AL) 10 November 1998 (1998-11-10)

2 INDEPENDENT CLAIM 1

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 does not involve an inventive step in the sense of Article 33(3)PCT.

2.1.1 Document D1 discloses (the references in parenthesis applying to this document):
an ophthalmic device comprising a sensor using diffraction for monitoring an analyte level in ocular fluid (paragraph 19 and 24).

2.1.2 The subject-matter of independent claim 1 differs from the disclosure of D1 in that:
the sensor is hologram-based.

2.1.3 The problem to be solved by the present invention may therefore be regarded as

to use a hologram as diffractive element for the detection of the analyte, where the hologram is biocompatible and stable over a long period of time.

2.1.4 In view of D2 the solution proposed in claim 1 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons:
From D2 showing a holographic ophthalmic lens which is used as a corrective optical lens (page 3, paragraph 2) the skilled person knows that a hologram can be part of an ophthalmic lens. Holographic optical elements have significant advantages in ophthalmic use (page 2, last paragraph - page 3, paragraph 1). Therefore the person skilled in the art would replace the diffractive element in the device of D1 by the hologram of D2 where circumstances make it desirable without making an inventive step.

3 INDEPENDENT CLAIM 11

3.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject matter of claim 11 does not involve an inventive step in the sense of Article 33(3)PCT.

3.1.1 Document D2, which is considered to represent the most relevant state of the art to the subject matter of claim 11, discloses (the references in parenthesis applying to this document):
introducing a crosslinkable fluid material into a cavity formed by a mold, wherein the mold consists of a female half and a matching male half, and the fluid material is exposed to laser radiation in order to produce interference fringe pattern (page 12, example).

3.1.2 The subject-matter of independent claim 11 differs from the disclosure of D2 in that :
the crosslinkable material comprises a molecular sensing moiety for detecting an analyte.

3.1.3 As argued above (see 2) it would be obvious to the skilled person to make a

sensor comprising a holographic element. From D1 it is known to use a polymer comprising a sensing moiety for making a sensor (paragraph 4). Consequently the skilled person would modify the material by using the teaching of D1 in the manufacturing process of D2 and inevitably arrive at the method of claim 11 without the exercise of inventive skill.

4 INDEPENDENT CLAIM 32

4.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 32 does not involve an inventive step in the sense of Article 33(3) PCT.

4.1.1 Document D2, which is considered to represent the most relevant state of the art to the subject matter of claim 32, discloses (the references in parenthesis applying to this document):
introducing a crosslinkable fluid material into a cavity formed by a mold, wherein the mold consists of a female half and a matching male half, and the fluid material is exposed to laser radiation in order to produce interference fringe pattern (page 12, example).

4.1.2 The special method of spraying a polymerizable fluid material on a surface for forming in a further step a hologram in the sprayed layer is merely one of several straightforward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill, in order to solve the problem posed (see e.g. D5, claim 7).

5 INDEPENDENT CLAIM 35

5.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 35 does not involve an inventive step in the sense of Article 33(3) PCT.

5.1.1 Document D2, which is considered to represent the most relevant state of the art to the subject matter of claim 35, discloses (the references in parenthesis applying to this document):

a method for making an ophthalmic lens comprising the steps of providing a mold consisting of two halves forming a cavity, depositing a crosslinkable fluid material in the mold, producing and recording an interference pattern in the fluid material while polymerizing, depositing again crosslinkable fluid material into the cavity and polymerizing the second fluid material whereby a single lens is formed (page 12, example; claim 7 and 8).

5.1.2 The special feature of using a polymerizable material comprising a molecular sensing moiety corresponds to claim 11 and for the same reasons (mutatis mutandis) claim 35 is not inventive.

6 INDEPENDENT CLAIM 50

6.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 50 is not new in the sense of Article 33(2) PCT.

6.1.1 Document D1 discloses (the references in parenthesis applying to this document)
a fluid composition comprising a prepolymer and a molecular sensing moiety, which san interact with an analyte to provide an optical signal (paragraph 18, 24, and examples).

6.2 Furthermore, even if it could be argued that the material of D1 would not be suitable for recording holograms, the present application would still not meet the criteria of Article 33(1) PCT, because the subject matter of claim 50 does not involve an inventive step in the sense of Article 33(3)PCT.

6.2.1 Document D2, which is considered to represent the most relevant state of the art to the subject matter of claim 50, discloses (the references in parenthesis applying to this document):
a fluid composition for making a biocompatible ophthalmic lens with a hologram comprising a prepolymer (page 4, paragraph 1 - page 5, paragraph 1).

6.2.2 The subject-matter of independent claim 50 differs from the disclosure of D2 in that :

the crosslinkable material comprises a molecular sensing moiety for detecting an analyte.

6.2.3 In view of D1 the solution proposed in claim 50 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons:
D1 shows a glucose sensor made of a polymerized material including a molecular recognition component (paragraph 20). The skilled person would therefore include the teaching of D1 in the device of D2 without making an inventive step.

7 DEPENDENT CLAIMS 2-10,12-31,33,34,36-49,51-63,65,66

7.1 Dependent claims 2-10,12-31,33,34,36-49,51-63,65,66 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step (Article 33(2) and (3) PCT).

7.1.1 Claim 2,3,5,8,23,45,61: Document D1 also discloses the use of a contact lens (paragraph 19), glucose as analyte (paragraph 19), a polymerized material comprising a molecular recognition component (paragraph 4), and phenyl boronic acid derivatives as molecular recognition component in the glucose sensor (paragraph 21).

7.1.2 Claim 4: in accordance with the circumstances a reflection hologram is the only type of hologram the skilled person would consider using, without the exercise of inventive skill, in order to solve the problem posed.

7.1.3 Claim 6,7,16-19,22,34,39,40,41,44,51,55-57,60: The crosslinked or polymerized materials made from water-soluble prepolymers are known as material for contact lenses, e.g. from Document D3.

7.1.4 Claim 9,10,24-26,38,46,47,52-54: The fact, that high refractive index differences are achieved by choosing polymers with aromatic groups is known (see e.g. D6, col 5 line 61-63).

7.1.5 Claim 12,36: It is a standard method to produce a reflection hologram by interference of two coherent light beams.

7.1.6 Claim 13-15, 33: From D4 it is known to partially polymerize a mixture before recording a fringe pattern (col 13, line 14-31). The methods for achieving the partially polymerization in claim 14 and 15 are merely two different straight forward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill, in order to solve the problem posed.

7.1.7 Claim 20,21,42,43,58,59: these water-soluble prepolymers are merely some of several straightforward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill, in order to solve the problem posed.

7.1.8 Claim 27,28,30,31,48,49: as the methods for producing a biocompatible sensor of claim 11,29,34 are not inventive, the sensors produced are mutatis mutandis also not inventive.

7.1.9 Claim 29,37: using a mirror on or behind a molding surface to reflect light and using the reflected beam together with the incident beam to form the interference pattern for the reflection hologram is a straightforward possi bility the skilled person would select.

7.1.10 Claim 62,63,65,66: as the ophthalmic device itself is not inventive, the use of such a device is mutatis mutandis also not inventive.